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**Serial N°:** 10/533,697

**Filed :** May 3, 2005

**Title :** New pyridopyrimidinone compounds, a process for their preparation and pharmaceutical compositions containing them

**Art Unit :** 1624

**Examiner :** JAISLE

Honorable Commissioner of Patents and Trademarks  
Washington, D.C. 20231

**DECLARATION UNDER 37 CFR 1.132**

I, SYLVAIN RAULT, a citizen of France, of Route de Saint-Pierre sur Dives 14370 MOULT, France, declare and say that :

I hold the degree of Doctor of Sciences from the University of Caen, France, in 1982, and I became Professor in this University in 1986.

Since 1998, I was appointed as Director of the " Centre d'Etudes et de Recherche sur le Médicament de Normandie " at the University of Caen, France. Between 1988 and 1998, I was Dean of the Faculty of Pharmacy in this University.

I am the author or co-author of 30 patents, 280 scientific publications and about 500 communications.

I am one of the co-inventors of US Patent Application Serial n° 10/533,697 filed May 3, 2005 concerning " New pyridopyrimidinone compounds, a process for their preparation and pharmaceutical compositions containing them ".

I am thoroughly familiar with the above-mentioned patent application and fully support the pharmacological experiments contained therein which were performed either by me or under my supervision. I also fully support the conclusions derived and the arguments presented as concerns the therapeutic interest of the compounds described.

The compounds of the present invention, being active on Src kinase, they could be used in the treatment of cancers.

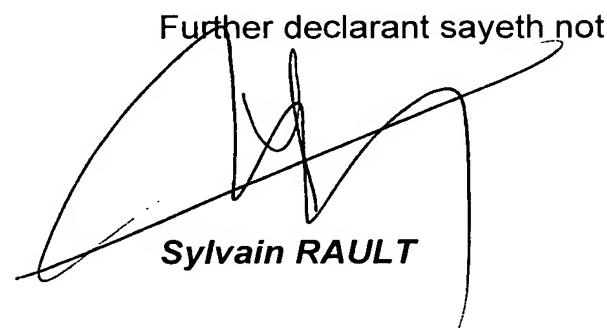
The compound disclosed at the example 7 in the present application (US Serial 10/533,697) exhibits a  $K_i$  coefficient of 1.67  $\mu\text{M}$  on Src kinases by using the conventional screening methods and by employing commercially available kinases.

This result is predictive of the potential use of this compound and of compounds with analogous structure in the treatment of many tumours. This is supported in the literature by the fact that the Src family of tyrosine kinases comprises eight related enzymes of which Src and Yes are the most studied in oncology. These kinases are found de-regulated and highly activated in more than eighty percent of solid tumours and many types of leukemias<sup>1,2</sup>. For example, in colon cancer, abnormal Src activity correlates with progression of disease to the metastatic state. In liver metastasis, Src activity can be as high as fourty-times the activity found in healthy tissue. For these reasons, inhibition of Src activity is accepted widely in the academic world and the pharmaceutical industry as a valid strategy against metastatic solid tumours. Since Src is an intracellular enzyme, small molecule chemical inhibitors are favoured compared to antibody-based strategies. Small molecule Src kinase

inhibitors are currently being tested by pharmaceutical companies in clinical trials showing promising results.

All these experimental and clinical data support the statement that the compounds of the present invention, active on Src kinases, should have a broad therapeutic potential in the treatment of cancers.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under section 1001 of the title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.



Further declarant sayeth not  
**Sylvain RAULT**

Executed at : Courbevoie

Date : 5/12/2006

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## REFERENCES

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(2) Summy JM, Gallick GE.

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